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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/776,537	02/02/2001	William Stern	P/546-236	1144

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EXAMINER	
HAGHIGHATIAN, MINA	

ART UNIT	PAPER NUMBER
1619	

DATE MAILED: 12/20/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/776,537	Applicant(s) STERN, WILLIAM	
	Examiner Mina Haghighatian	Art Unit 1619	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 June 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 16, 18 and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The use of the trademark Tween 80 has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. The use of trademarks in claims is not permissible.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-4, 6-14 and 16-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mardente et al (6,149,893) in view of Cho et al (5,665,700).

Mardente teaches pharmaceutical compositions for intranasal administration containing in a spray dosing feeder calcitonin dissolved in a substantially physiological solution for sodium chloride adjusted to a pH between 3.5 and 4.5 with citrate buffer and hydrochloric acid without any preservative. The preferred type of calcitonin is the salmon calcitonin, also known as salcatonin, and the therapeutically effective amounts are between 500 and 2500 I.U. of calcitonin for each milliliter of solution, meeting instant claims 1-4 and 6-14 (col. 1, line 1 to col. 2, line 37).

Mardente also discloses that it was found surprisingly that pharmaceutical compositions for the intranasal administration containing calcitonin in an aqueous solution of sodium chloride adjusted to pH between 3.5 and 4.5 with citrate buffer and hydrochloric acid possess the same bioavailability and preservation as the compositions of calcitonin containing preservatives and/or absorption-increasing agents, thus meeting instant claim 23. Also disclosed is that the citrate buffer is used to give a better stability of the pH of the solution during the period of validity of the product, thus meeting instant claim 22 col. 1, line 63 to col. 2, line 12).

Examples 1-2 describe the process of making the spray pharmaceutical composition and indicate the concentration ranges. Mardente lacks specific teachings on Tween 80 and some preservatives.

Cho teaches a pharmaceutical formulation comprising a biologically active material such as insulin, calcitonin, etc. The emulsification aids, such as polysorbate 80, are present in an amount enough to assist in adequately obtaining a stable formulation. The preferred amount is 0.1 to 5% w/v of the formulation, thus meeting instant claim 16-19 (col. 9, lines 19-37). Antimicrobial preservatives which may be used generally from about 0.5 to 2.5% w/v, of the total formulation, include methylparaben, ethylparaben, propylparaben, butylparaben, phenylethyl alcohol, benzyl alcohol, etc, thus meeting instant claim 17-19 (col. 10, lines 4-12).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to have modified the composition of Mardente of a intranasal pharmaceutical composition containing salmon calcitonin, using composition of Cho, containing calcitonin and emulsifiers and preservatives, because of the expectations of preparing a composition that is more effective, stable but causes less irritations. Furthermore, it would have been obvious to a person of ordinary skill in the art, given the optimum pH levels for a composition, to have adjusted the concentration of the bases and the acids in the composition to reach the desired pH levels.

Claims 5 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mardente and Cho as applied to claims 1-4, 6-14, 16-23 above, and further in view of Dua et al (International Journal of Pharmaceutics 1997).

Mardente and Cho were discussed above. The combined references lack specific teachings on viscosity and osmolarity of the composition.

Dua et al discloses the influence of tonicity and viscosity on the intranasal absorption of salmon calcitonin in rabbits. In this study formulations were designed as nasal sprays with viscosity at 1 and 76 cps, and a tonicity of 100, 300 or 600 mOsms. The results indicated that the deviations from isotonicity increased the bioavailability by 4-5 times. Variation in the viscosity did not influence the bioavailability of salmon calcitonin (see abstract and pages 237-241).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to have modified the compositions of the combined references, using the teachings of Dua, with the reasonable expectations of preparing an intransal preparation of salmon calcitonin with the optimum viscosity and tonicity levels to improve bioavailability and effectiveness.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mina Haghighatian whose telephone number is 703-308-6330. The examiner can normally be reached on core office hours.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Diana Dudash can be reached on 703-308-2328. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0198.

Mina Haghighatian
Patent Eaxminer
December 14, 2001

DIANA DUDASH
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